AETC AIDS Education & Training Center Program Mountain West

"IM" Thinking About Using Long-Acting Injectables…

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echo

Disclosures

Nothing to disclose

Objectives

- Consider potential pros and cons of switching to intramuscular (IM), long-acting cabotegravir-rilpivirine (LA CAB-RPV) for an individual with suppressed viral loads
- Review contraindications to LA CAB-RPV and factors that may predict worse outcomes
- Format for debate: case, then poll, followed by presentation of ”pro” side then “con” side, then repeat poll, then discuss

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Case

- "L.A." is a 50-year-old male diagnosed with HIV in 2005. He initially took EFV/FTC/TDF (*Atripla*) and did well until he experienced virologic failure in 2015 due to missed doses. He developed a K103N mutation and switched to DTG/ABC/3TC (*Triumeq*). He has some CVD risk factors, struggles with the large pill size, and misses some doses. Since switching to DTG/ABC/3TC he has had some low-level viremia but the HIV RNA has now been <50 copies/mL for over a year. He does not have hep B.
  - Other meds: lisinopril 20 mg daily, atorvastatin 10 mg
  - PMH: HTN, hyperlipidemia, obesity (BMI 32)

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Poll

- POLL: Would you recommend this patient switch to LA-CAB/RPV to manage his HIV?

  A) Yes
  B) No

Pro-Switch

Brian R. Wood, MD

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Reasons to Vote Yes for IM CAB-RPV

- It works! Very effective with excellent long-term data
- It's safe! Avoids all NRTI toxicity and serious AE's rare
- It's easy! Monthly dosing (every 2-month option coming)
- It's preferred! People with HIV consistently prefer it

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IM CAB-RPV Works!
Key Phase 3 Studies & Duration of Follow Up

- Treatment-Naïve Individuals

  FLAIR: IM CAB-RPV monthly vs. oral DTG-ABC-3TC daily: 124 weeks[1]

- Treatment-Experienced Individuals

  ATLAS: switch to monthly IM CAB-RPV vs cont. 3-drug ART: 96 weeks[2]

  ATLAS-2M: switch to IM CAB-RPV every 4 or 8 weeks: 96 weeks[3]

- Ongoing

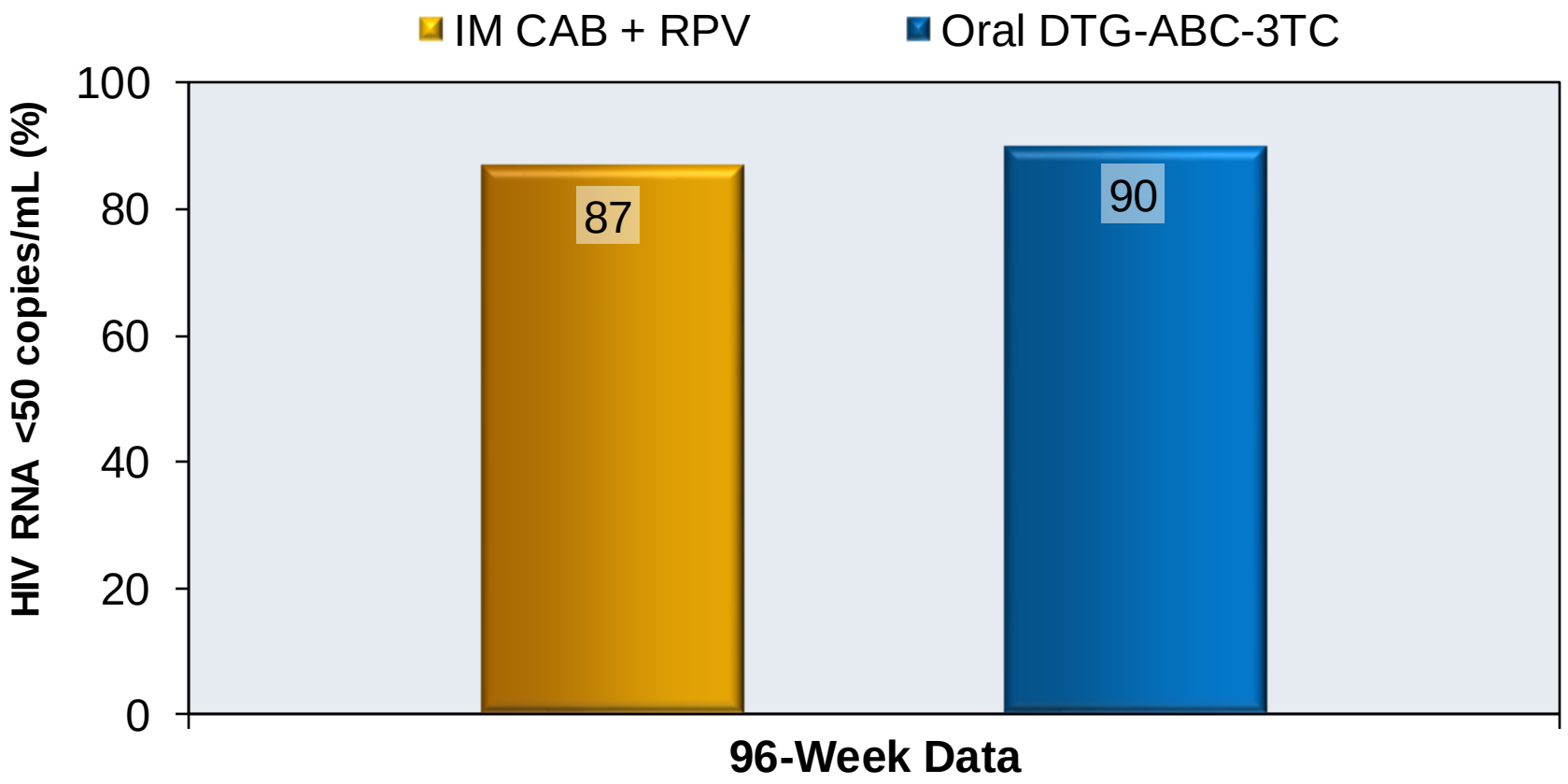
  MOCHA: LA CAB-RPV for children and adolescents

  SOLAR: switch to every 8 week IM CAB-RPV vs continue BIC-FTC-TAF

  LATITUDE: IM CAB-RPV vs oral ART with history of adherence issues

1. Orkin. IAS 2021. Abstr OAB030 2. Swindells S et al. AIDS 2021. 3. Jaeger H et al. CROI 2021.

FLAIR: 96-Week Results
IM CAB-RPV Monthly vs Oral DTG-ABC-3TC for Initial ART



*HIV RNA ≥50 copies/mL at 96 weeks: n = 9 (3%) CAB-RPV, n = 9 (3%) DTG-ABC-3TC
*Resistance: 3 virologic failures with resistance in CAB-RPV arm (all from Russia, A1 virus)

Orkin C, et al. Lancet HIV. 2021;8:e185-e196.

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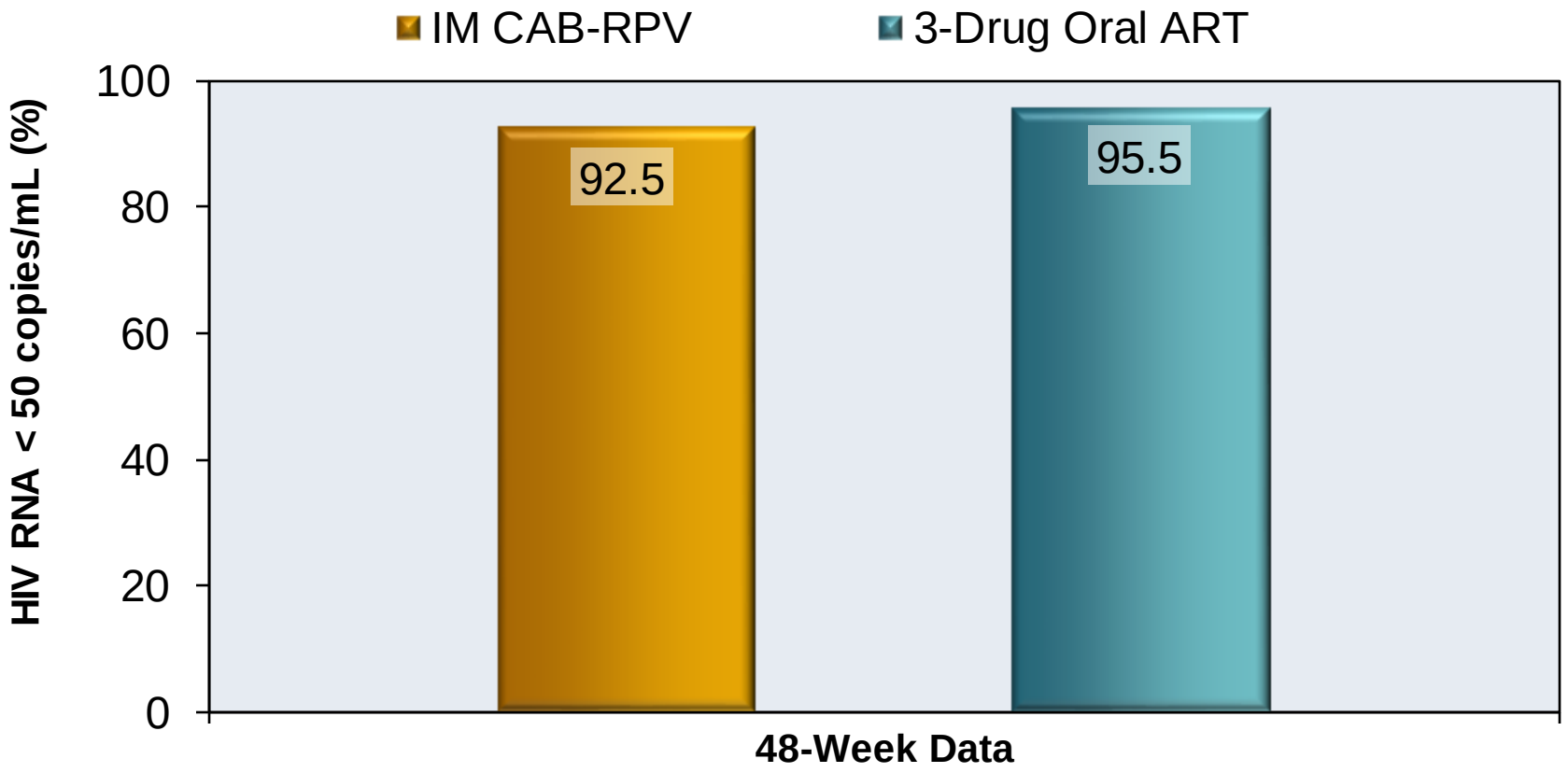
ATLAS Study: 48-Week Results
Switch to IM CAB-RPV Monthly vs Continue Daily Oral ART



*HIV RNA ≥50 copies/mL at 48 weeks: 1.6 % CAB-RPV, 1.0% 3-drug oral ART
*Resistance: 3 virologic failures with resistance in CAB-RPV arm (2 from Russia, A1 virus)

Swindells S, et al. N Engl J Med. 2020;382:1112-23.

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IM CAB-RPV: Safe and Well Tolerated!

- Injection site reactions common but mild & short-lived:
  - 89% grade 1, 11% grade 2[1]
  - Median duration 3 days[1]
- Adverse events leading to withdrawal quite rare:
  - FLAIR: n = 3 (1%) IM CAB-RPV, n = 4 (1%) DTG/ABC/3TC[1]
  - ATLAS: withdrawal due to injection site reaction: n = 4 (1%)[2]
- PLUS, no abacavir and no tenofovir!

1. Orkin C, et al. Lancet HIV. 2021;8:e185-e196. 2. Swindells S, et al. NEJM 2020.

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Long-Acting ART: Preferred!

- Greater improvements in treatment satisfaction and acceptability in FLAIR and ATLAS in LA arm compared to oral arm[1]
  - ATLAS: all switch arm participants (100%) surveyed preferred LA therapy to their previous daily oral regimen[2]
- Reported benefits:[3,4]
  - Convenience (e.g., no carrying pills when traveling)
  - Improved quality of life
  - Reduced stigma
  - Elimination of daily reminder of HIV, reduced emotional burden
  - Better for swallowing/GI difficulties
  - Reduced confidentiality/privacy concerns
  - 50% felt it would improve adherence

1. Murray M et al. AIDS Behav 2020. 2. Swindells S et al. AIDS 2021. 3. Kerrigan D et al. PloS One 2018. 4. Akinwunmi B et al. Sex Trans Infect 2021.

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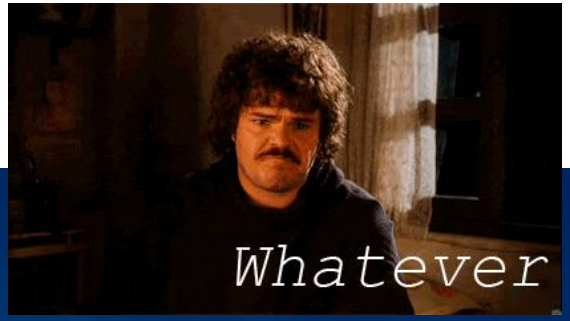
Now, for the opposing side…

Not so fast my friend….
David Hachey, PharmD



Three reasons *not* to switch

https://en.wikipedia.org/wiki/Neapolitan_ice_cream

Before Starting Therapy (Vanilla)

- Data - it is effective and safe…but for everyone?
  - Originally rejected by the FDA due to issues related to chemistry, manufacturing, and controls (CMC)
  - 34-40 yo white men with a normal BMI
    - Women of child-bearing potential and obesity??
  - Avoiding TAF/ABC
    - Discuss other oral options such as DTG/RPV and DTG/3TC
  - Drug interactions
    - Avoid several interactions with the injection, but strong inducers can lower levels of ART significantly
  - Excluding injection site reactions, still significantly higher rates of adverse drug reactions
    - Consider Torsade de Pointes in patients who may be on other medications (or be placed on these medications)

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

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Before Starting Therapy (Vanilla)

Drug-Related Adverse Events and Injection Site Reactions (ISR)		
Drug-Related Adverse Event (AE)	**IM CAB + RPV** (n = 283)	**DTG-ABC-3TC** (n = 283)
Any AE	236 (83)	28 (10)
Any AE, excluding ISR	79 (28)	28 (10)
Grade 3 or 4 AE	14 (5)	0
Grade 3 or 4 AE, excluding ISR	4 (1)	0
Any injection site pain	227 (80)	NA

Source: Orkin C, et al. N Engl J Med. 2020;382:1124-35.

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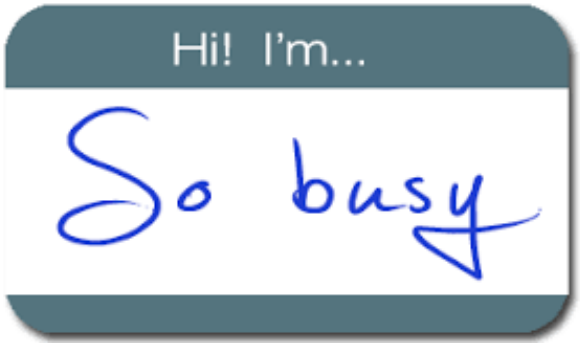
Starting Therapy (Chocolate – most important)

Access



- **The "Busy Badge"**
  - Patients' ability to get labs and see a a provider every 6 months is challenging
  - Clinics are often understaffed, overworked, and don't always have the personnel to manage coordinating who is on what and who needs injections when
  - Rurality of our patient population
  - Attending to these patients will take resources away from patients who really need nursing and provider attention
- **Navigating Medication Acquisition**
  - More paperwork, medication storage, prior authorizations, etc…
- **CUSTOMIZE trial**
  - Conducted by ViiV to assess **<u>perceived and actual</u>** barriers by healthcare teams
  - Respondents (N=26) indicated they felt LAI was acceptable, appropriate and feasible, but significant barriers exist

http://programme.aids2020.org/Abstract/Abstract/10530

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CUSTOMIZE Trial

	Perceived Barrier at Baseline N=26, %*	Actual Barrier at Month 4 N=24, %*
Patient ability to keep monthly appointments	80.8	37.5
Patient transportation for monthly appointments	76.9	37.5
Flagging/awareness of missed injection visits	73.1	45.8
Staff Resourcing for clinic flow	53.8	37.5
Rescheduling missed injections	50.0	20.9
Patients failing CAB+RPV LA due to missed doses/injection visits	50.0	16.6
Management of patients presenting to injection visits with other care needs	50.0	33.4
Patient injection pain/soreness	46.1	41.7

http://programme.aids2020.org/Abstract/Abstract/10530

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The leftovers (Strawberry)

- Does this create more 'inequality' in medicine??
  - "…this major advance in treating HIV infection will provide a new option for a **select** group of patients who currently have viral suppression while taking ART and represents the first step toward making less-frequent dosing of ART a reality."
  - What about women of child-bearing potential, PWID, people dealing with housing instability, rural patients, relocating or traveling, etc…
- Switching back and forth from LAI to oral
  - This will become a reality based on changes in insurance, availability from pharmacies, non-adherence, and new meds
  - How do we handle virologic failures?
- Monitoring and follow up (see chocolate)
  - Most patients want to be seen less…not more often

Currier JS. N Engl J Med 2020; 382:1164-1165

Long-Acting ART: Be careful for what you wish for!

- Original denial from the FDA
- Other options for NRTI sparing regimens
- Drug interactions still exist
- Higher rates of side effects compared to oral therapy
- Increased staff/provider burden
- Inconvenience for patients to come to clinic monthly
- Driving inequality in health care

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Review & Discussion

Case

- "L.A." is a 50-year-old male diagnosed with HIV in 2005. He initially took EFV/FTC/TDF (*Atripla*) and did well until he experienced virologic failure in 2015 due to missed doses. He developed a K103N mutation and switched to DTG/ABC/3TC (*Triumeq*). He has some CVD risk factors, struggles with the large pill size, and misses some doses. Since switching to DTG/ABC/3TC he has had some low-level viremia but the HIV RNA has now been <50 copies/mL for over a year. He does not have hep B.
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Cabotegravir and Rilpivirine (*Cabenuva*) *Extended Release Injectable Suspension: Reminders*

- **Indication**
  - Replace ART regimen in persons with HIV RNA <50 copies/mL
  - Taking stable ART regimen
  - No history of treatment failure
  - No known or suspected resistance to cabotegravir or rilpivirine
  - No hepatitis B co-infection
- **Additional considerations**
  - Insurance coverage
  - Ability to attend clinic monthly
  - Drug-drug interactions
  - Other predictors of virologic failure: BMI >30, HIV subtype A6/A1 (associated with integrase polymorphism L74I)[1,2]

Sources: Cabenuva Prescribing Information
1. Cutrell A et al, AIDS 2021. 2. Charpentier C et al, J Antimicrob Chemother 2021.

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Cabotegravir and Rilpivirine (*Cabenuva*) *Dosing Schedule*

Oral Lead-In x 1 month (≥28 days)

Cabotegravir 30 mg daily +
Rilpivirine 25 mg daily

***Initiation Injections (x 1)**

Cabotegravir (600 mg): 3 mL IM +
Rilpivirine (900 mg): 3 mL IM

***Continuation Injections (Monthly)**

Cabotegravir (400 mg): 2 mL IM +
Rilpivirine (600 mg): 2 mL IM

*Administer injections at opposite gluteal sites (or at least 2 cm apart) and give both during the same visit.

*See prescribing guidelines or National HIV Curriculum for guidance on missed doses (planned or unplanned)

Source: Cabenuva Prescribing Information

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